Journal of
Cardiology & Cardiovascular
Surgery

Original Article

DOI: 10.51271/JCCVS-0054

Comparison of Pan-Immune Inflammatory Index in patients dialysed from catheters and fistulas

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Cite this article: Öztürk H, Felek D, Varlıbaş A, Hacıömerlioğlu A, Öztürk ZN, Çifci A. Comparison of Pan-Immune Inflammatory Index in patients dialysed from catheters and fistulas. *J Cardiol Cardiovasc Surg.* 2025;3(2):29-34.

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Received: 28/05/2025 ◆ **Accepted**: 25/06/2025 ◆ **Published**: 27/06/2025

ABSTRACT

Aims: Chronic kidney disease is a group of diseases associated with inflammatory processes, and the risk increases as the stage progresses. Increased inflammation in the disease is associated with mortality and morbidity, and diagnosis and treatment are very important. Arteriovenous fistula is recommended as the first choice for hemodialysis access. Some patients dialysed from catheters. We predict that catheters may cause a chronic inflammatory condition, and we planned this study to demonstrate this.

Methods: 242 patients from dialysis patients who applied to Kırıkkale University Internal Medicine Clinic, Ankara Private Balgat Dialysis Center and Yozgat Bozok University Internal Medicine Clinic were included in the study; demographic data (age, gender), history data (chronic diseases, continuously used medications), data regarding hemodialysis duration, laboratory data (HGB, WBC, PLT, MPV, neutrophil, monocyte, lymphocyte, C-reactive protein, urea, creatinine, glomerular filtration rate) of the patients were recorded. Pan-Immune Inflammatory Index (PII) ((neutrophil count x platelet count x monocyte count)/lymphocyte count) were calculated. Differences between hemodialysis vascular access and PII values were statistically analyzed in SPSS package program.

Results: According to hemodialysis vascular access routes, it was found that 182 (75.2%) of the patients had fistula dialysis, 60 (24.8%) had catheter dialysis and 85% of the individuals on catheter hemodialysis had permanent catheters, 15% had temporary catheters, 88% had jugular, and 12% had subclavian and femoral catheters. Inflammation levels were calculated with PII. While PII was calculated as 21125.33±39621.37 in patients undergoing hemodialysis through fistulas, it was calculated as 29745.24±50905.25 in patients undergoing hemodialysis through catheters (p=0.037*). In correlation analyses; A strong positive correlation was observed with lymphocyte, monocyte, neutrophil and platelet counts (respectively; 0.242**, 0.871**, 0.888**; 0.365**). A weak negative correlation was found with the duration of chronic kidney disease (-0.242*).

Conclusion: Since there is no directly related parameter developed for analyzing the level of inflammation, there is a need for formulation methods. PII is also a tool used for this purpose. In our study, we analyzed in which cases the increased oxidative stress in hemodialysis is higher with PII and the parameters that trigger it, and as a result, we found higher inflammation in patients hemodialyzed from catheters compared to patients hemodialyzed from fistulas. We concluded that the increased oxidative stress in chronic kidney disease can be further removed from the fistula by hemodialysis or that oxidative stress caused by foreign bodies such as catheters may be higher. For a more definitive decision, further examination is needed by evaluating before and after hemodialysis and examining individuals with chronic kidney disease who are on hemodialysis and those who are not.

Keywords: Chronic kidney disease, inflammation, Pan-Immune Inflammatory Index, catheter, fistula

INTRODUCTION

Chronic kidney disease is a disease that causes systemic inflammatory processes; as the stage of the disease progresses, inflammation increases. Increasing inflammation in stage-5 dialysis patients has brought many problems with it.[1,2] Realizing and preventing this situation, which is quite difficult to detect, will contribute positively to mortality and morbidity.[3] The reference ranges of C-reactive protein, one of the indicators of inflammation, have also become open to interpretation as the stage progresses in chronic kidney disease. However, since biomarkers such as C-reactive show a more significant increase in infection as well as inflammation, the need for new biomarkers to detect infection-related inflammation has increased.[4] Although there are many biomarker studies on this subject in the literature, many of

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them have not been routinely used in clinical practice due to factors such as effective results and cost.[5] For this reason, it is still very valuable to detect inflammation with routinely studied tests in clinical practice.

Many studies have been conducted on inflammation in chronic kidney disease, such as hemopoietic cells, vitamin levels, nutritional status, and the presence of nutrition.[6,7] However, most of them have been treated by physicians, some of which are treatable and some of which are incurable. The modifiable factors of dialysis are; method, vascular access route, dialysate, dialyzer, and when these are examined, not every method is suitable for every patient, but the more widespread use of hemodialysis compared to peritoneal dialysis has made it more possible to investigate this group.[8,9] Various vascular interventional methods are used during dialysis treatment. The first of the two main methods is the use of a catheter in hemodialysis treatment, which allows blood to be taken out of the body, and the fistula method, which allows blood to return to the body by opening a direct vascular access.[10,11] These two methods can significantly affect patients' compliance with treatment, quality of life, and long-term survival. However, there are some complications associated with both methods and inflammatory processes that can affect the immune system.[12] During hemodialysis applications, some systemic inflammatory responses can be observed with both methods used. These responses can affect the response of patients to treatment, the development of infection, vascular occlusion and other cardiovascular complications. Therefore, evaluating the effects of both treatment methods on inflammatory processes is important for an optimal approach in the treatment process.[13]

Pan-Immune Inflammatory Index (PII) ((neutrophil count x platelet count x monocyte count)/lymphocyte count) is a tool used to measure systemic inflammation, and how this indicator changes in patients receiving dialysis treatment is an important research question. Whether catheter and fistula use have different effects on this inflammatory index can provide important information about the treatment processes of patients. Although fistula use is generally seen as longer lasting and less complicated, dialysis treatment with catheters is preferred for some patients because it provides faster access. The aim of the study is to better understand the advantages and disadvantages of both treatment methods by comparing their effects on inflammatory responses and to provide guidance for clinical applications.[14,15]

METHODS

Ethics

The study was initiated after obtaining ethics committee approval from Yozgat Bozok University Non-interventional Clinical Researches Ethics Committee (Date: 09.04.2025, Decision No: 457). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Patients and Methods

The retrospective study was planned to include dialysis patients who applied to Kırıkkale University Internal Medicine Clinic, Ankara Private Balgat Dialysis Center, and Yozgat Bozok University Internal Medicine Clinic between January 2025 and February 2025. A total of 242 individuals were included in the study. The data to be obtained within the scope of the study were obtained from anamnesis and clinical course forms. In addition, they were recorded from the hospital information system and laboratory system. Demographic data (age, gender), data regarding the past history (chronic diseases, continuously used medications), data regarding the duration of hemodialysis, laboratory data (HGB, WBC, PLT, MPV, neutrophil, monocyte, lymphocyte, C-reactive protein, urea, creatinine, glomerular filtration rate) were recorded. PII ((neutrophil count x platelet count x monocyte count)/lymphocyte count), a biomarker used to measure systemic inflammation, was calculated. Differences between hemodialysis vascular access and PII values were analyzed statistically.

Inclusion criteria: Patients over 18 years of age with a diagnosis of chronic renal failure and on routine hemodialysis for at least one year.

Exclusion criteria: Patients under 18 years of age, patients on temporary hemodialysis (such as acute renal failure, intoxication, electrolyte imbalance), patients with signs of active infection, pregnancy, breastfeeding, patients with active malignancy, patients with a known history of rheumatologic disease, patients with a history of renal transplantation, patients receiving anti-inflammatory medical treatment, and patients who had surgery within the last 3 months.

Statistical Analysis

Data were evaluated with SPSS 22.00 package program and descriptive statistics were expressed as number (n), frequency (%), mean (Mean), standard deviation (±SD) in statistical analyses. Kolmogorov-Smirnov test was used to analyze the normality distribution of the data. Chi-square test was used to compare categorical variables. Independent groups T-test was used to compare two groups for normally distributed data and nonparametric Mann-Whitney U Test was used for non-normally distributed data. Chi-square test was used to compare the data. Statistically, $p<0.05$ was considered significant.

RESULTS

According to hemodialysis vascular access routes, 182 (75.2%) of the patients were dialyzed via fistula, 60 (24.8%) were dialyzed via catheter, 85% of the patients with hemodialysis via catheter had permanent catheters, 15% had temporary catheters, 88% had jugular catheters, and 12% had subclavian and femoral catheters. The mean duration of hemodialysis due to chronic renal failure was 6.37 years. The mean glomerular filtration rate was calculated as 7.28. Of the 242 individuals included in the study, 145 (59.9%) were male and 97 (40%) were female. There was no statistically significant difference between the two genders. The mean age of the individuals included in the study was calculated as 63.53 years and there was no statistically significant difference between the groups in terms of age.

Monocyte, lymphocyte, neutrophil and platelet levels were recorded. No statistically significant difference was found between the hemogram findings of the two groups; the results of the analysis were calculated as p=0.731,

p=0.244, p=0.154, p=0.654, respectively. PII was calculated as 21125.33±39621.37 in patients receiving hemodialysis through fistula and 29745.24±50905.25 in patients receiving hemodialysis through catheter (p=0.037*) (**Table 1**).

Table 1. Comparison of general data and Pan-Immune Inflammatory Index with hemodialysis access route

	Fistula (n=182)		Catheter (n=60)		p
	Mean	STD	Mean	STD	
Age (years)	63.53	11.41	63.57	16.73	0.304
Disease duration of time	6.81	7.11	5.05	5.57	0.050
Lymphocytes	4.44	8.21	4.69	8.54	0.731
Monocytes	4.16	5.63	5.32	10.79	0.244
Neutrophils	27.50	28.63	33.57	31.94	0.154
Platelets	200.17	68.40	202.60	76.91	0.654
CRP	16.14	22.70	17.61	26.61	0.492
PII	21125.33	39621.37	29745.24	50905.25	0.037*

CRP: C-reaktif protein, PII: Pan-Immune Inflammatory Index

Inflammation levels were calculated with the PII. Inflammation was found to be higher in individuals receiving hemodialysis through catheter compared to individuals receiving hemodialysis through fistula (**Figure**).

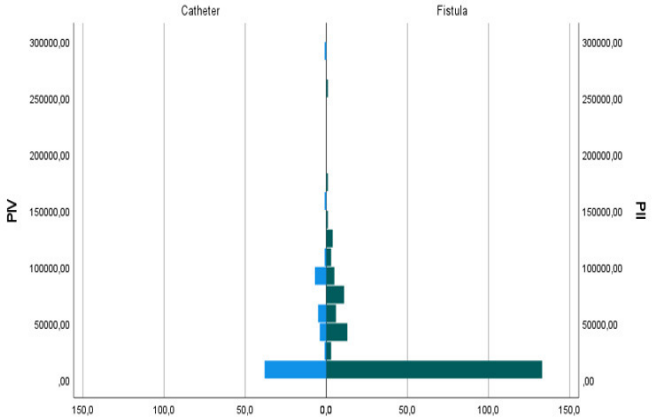

Figure. Hemodialysis vascular access route

PII (neutrophil count x platelet count x monocyte count)/ lymphocyte count) calculation is a formulation that is directly proportional to neutrophil, platelet and monocyte counts and inversely proportional to lymphocyte count. When the correlation results were evaluated in accordance with this formula, strong positive correlations were observed with monocyte, platelet and neutrophil counts, while positive correlations were observed with lymphocyte counts, as expected. In correlation analyses, strong positive correlations were observed between PII and lymphocyte, monocyte, neutrophil and platelet counts (0.242**, 0.871**, 0.888**, 0.888**, 0.365**, respectively). There was a weak negative correlation between duration of chronic kidney disease and PII (-0.242*) (**Table 2**).

When the presence of chronic diseases other than chronic kidney disease was evaluated, it was observed that 137 patients had diabetes mellitus and 153 patients had hypertension. When the relationship between each of these diseases and PII was evaluated separately, PII was calculated as 27533.12±49497.57 in individuals with diabetes mellitus and PII was calculated as 24809.33±43607.57 in individuals with hypertension; although PII was higher in the presence of chronic diseases, the data were not statistically significant (p=0.053; p=0.435; respectively) (**Table 3**).

DISCUSSION

Of the 242 individuals included in the study, 145 (59.9%) were male and 97 (40%) were female; the mean age of the individuals was calculated as 63.53±12.89 and there was no statistically significant difference between the groups in terms of age. The fact that there was no difference between the results of the statistical analysis in terms of age and gender increases the power of the study and the low effect rate of non-modifiable factors. In the most recent report of the Turkish Society of Nephrology, in which the practices and distributions related to hemodialysis across the country were given in 2023, the annual incidence of hemodialysis was calculated as 190.9 in men and 128.6 in women per million population, and it was observed that it was higher in men. It was also noted that the rate of hemodialysis increased with increasing age. In our study, the number of male patients was higher in the male gender in accordance with national data. In our study, 182 (75.2%) patients received dialysis from fistula and 60 (24.8%) from catheter, and 85% of the individuals who received hemodialysis from catheter had permanent catheters, 15% had temporary catheters; 88% had jugular, 12% had subclavian and femoral catheters. In our study, it was observed that the number of individuals receiving hemodialysis through fistula was higher than the number of individuals receiving hemodialysis through catheter and jugular vein was more preferred in the choice of vein for catheter. In the 2023 National Nephrology dialysis and transplantation registry report, it was found that arteriovenous fistula use was 26.58%, arteriovenous graft use was 0.18%, permanent catheter use was 51.44% and temporary catheter use was 21.80%.[16] Our patient profile showed a higher rate of fistula use, which is different from national data. In his evaluation of the vascular access route of hemodialysis patients in clinical practice, he drew attention to the selection of the appropriate method for the appropriate patient. He recommends fistula as the first choice because of the low risk of infection. Although there is evidence that the rate of hospitalization increases with the increased risk of infection caused by hemodialysis with central venous catheters, he concluded that there is insufficient evidence to explain the relationship with infection-induced hospitalization and consequently mortality. It emphasizes the importance of appropriate method and graft selection considering the risks of long-term vascular complications in fistulas.[17]

PII (neutrophil count x platelet count x monocyte count)/ lymphocyte count) calculation was formulated as directly proportional to neutrophil, platelet and monocyte count and inversely proportional to lymphocyte count. When our correlation results were evaluated in accordance with this formulation, we observed a strong positive correlation with monocyte, neutrophil and platelet counts as expected (0.871**, 0.888**, 0.365**, respectively), while the positive

Table 2. Correlation of Pan-Immune Inflammatory Index with general data and hemogram values

		CKD duration (years)	Lymphocyte	Monocyte	Neutrophil	Platelets	CRP	PII
CKD duration (years)	r							
	p							
Lymphocyte	r	-0.019						
	p	0.766						
Monocyte	r	-0.069	0.459					
	p	0.282	<0.001					
Neutrophil	r	-0.107	0.376	0.748				
	p	0.095	<0.001	<0.001				
Platelets	r	-0.065	0.298	0.215	0.255			
	p	0.316	<0.001	<0.001	<0.001			
CRP	r	0.108	0.029	-0.041	0.048	0.127		
	p	0.096	0.658	0.525	0.455	0.049		
PII	r	-0.127	0.242	0.871	0.888	0.365	<0.001	
	p	0.050	<0.001	<0.001	<0.001	<0.001	0.982	

CKD: Chronic kidney disease, CRP: C-reaktif protein, PII: Pan-Immune Inflammatory Index

Table 3. Association between Pan-Immune Inflammatory Index and chronic disease

	Yes	No	p
Diyabetes mellitus	27533.12±49497.57	17420.29±30566.12	0.053
Hypertension	24809.33±43607.57	20384.64±41076.65	0.435

correlation with lymphocyte count (0.242**) was thought to be due to the fact that other parameters in the hemogram were higher in individuals with higher lymphocytes. In inflammation, the increase in lymphocytes is not more than the increase in monocytes, neutrophils and platelets. In our study, the minimum duration of hemodialysis due to chronic renal failure was 1 year and the maximum duration was 55 years with a mean of 6.37 years. A weak negative correlation was observed between the duration of chronic kidney disease and PII (-0.242*), suggesting that hemodialysis due to chronic renal failure reduces inflammation in the long term. Increased inflammation due to chronic renal failure is removed from the body by long-term hemodialysis and further investigation with data related to the frequency of hemodialysis is needed. Inflammation in chronic kidney disease is quite high and the factors that increase and decrease it have been investigated. Because it has been observed that inflammation increases mortality and morbidity.[18] In fact, inflammation has been one of the factors blamed for fibrosis in the clinical course of chronic kidney disease.[19] In our study, we examined the effect of catheter and fistula on systemic inflammation in the group in which end-stage inflammation was considered to be high rather than stage-related inflammation and we found that inflammation was higher in individuals receiving hemodialysis through catheter compared to individuals receiving hemodialysis through fistula. Many studies have addressed infection-related inflammation in hemodialysis patients with catheters.[20] However, it has been concluded that the catheter can be almost as safe as the fistula in patients with clean and regular care and can be used safely in pregnant women when hemodialysis is necessary. However, it was still emphasized that the safest method should be preferred by informing about vascular access methods before pregnancy.[21] As a result, it was expected that the catheter with a foreign body increased the infection rate by forming a biofilm layer and the associated inflammation was found to be high.[22] However, in our study, we tried to minimize the effect of infection-related inflammation by studying in patients with no evidence of active infection. As a result, we observed that inflammation was high in the patient group with catheter even if there was no current infection. This result proved that there was a qualitative data proving that there was a condition related to inflammation caused by the foreign body. In the study conducted by Çantay et al.[23] in the gastrointestinal system, data on inflammation caused by foreign body were obtained and local inflammation was mentioned. However, the inflammation caused by a foreign body such as a catheter, which was present for a long time in our study, is expected to be more widespread and may reach detectable levels in systemic terms. On the other hand, the results of the analysis also raised the question of whether the catheter would be less effective than the fistula in clearing the existing inflammation. Because according to the analysis results found in the literature, many biomarker studies have been conducted to evaluate inflammation. Malyszko et al.[24] study on inflammation-associated neutrophil genatinase; Doğan et al.[25] study on Apelin 13; Mohammed et al.[26] study on asymmetric dimethylarginine. It is obvious that these and similar biomarkers have no place in clinical practice. Because high cost and effective results limit the use of these and similar biomarkers. However, in addition to these biomarkers, prediction of inflammation with the results of routine analysis has also been the subject of the literature. The use of leukocyte-related inflammation index not only in hemodialysis patients but also in tremor and studies on inflammation prediction with hematologic laboratory data in patients with lupus are examples.[27,28] Studies have also been conducted in chronic kidney disease and there are studies on additional systemic inflammatory index.[29,30] Unlike the existing studies, our study also examines the relationship of the known increased inflammation with the vascular access route and the duration of chronic kidney disease. The finding

that inflammation was higher with increasing duration of chronic kidney disease did not show that the presence of a catheter increased inflammation more than a fistula, but supported that the catheter could not remove inflammation-related toxins as well as the fistula.

When the etiologic factors of hemodialysis patients were analyzed in our study, it was observed that diabetic and hypertensive nephropathy were the major etiologic factors. Although PII was found to be higher in the presence of chronic diseases other than chronic kidney disease, the data were not statistically significant. This result again increases the power of the study in the relationship between chronic kidney disease and PII. According to national nephrology registry data, diabetes mellitus rate was 34.87% and hypertension rate was 24.42% in individuals undergoing hemodialysis due to end-stage renal failure in our country; however, the frequency of hypertension was found to be higher in our patient profile.[16] In the literature, there are studies evaluating the presence of chronic disease and PII and in the study by Tuzimek et al.[31] no significant difference was observed in the systemic inflammation index used to predict acute coronary syndrome in diabetic patients. In the study by Huang et al.,[32] a positive correlation was observed between fragility fracture in postmenopausal anemic women with type 2 diabetes, indicating that the systemic inflammatory index is a useful tool in predicting this condition. Xiu et al.[33] evaluated the use of the systemic inflammation index as a predictive factor in hypertension follow-up and concluded that it can be used as an early warning parameter in the determination of mortality and poor prognosis. It has been observed that systemic inflammation index has a wide range of studies in chronic diseases.

CONCLUSION

Inflammation is a problem that occurs in many diseases and conditions and it is very important to detect, prevent and attempt to reduce it. Unfortunately, it is not yet possible to predict the level of inflammation with a single biomarker. Since there is not yet a directly related parameter developed to analyze the level of inflammation, the need for formulation methods is obvious. In our study, PII was used for inflammation assessment. PII is a value calculated by neutrophil count x platelet count x monocyte count)/ lymphocyte count and has been proven to increase in inflammation. In our study, we analyzed in which conditions the oxidative stress increased in hemodialysis with PII is higher and what are the parameters that trigger it, and as a result, we found that inflammation was higher in patients undergoing hemodialysis through catheter compared to patients undergoing hemodialysis through fistula. It was thought that the increased oxidative stress in chronic kidney disease may be further removed by hemodialysis through fistula or inflammation caused by foreign body such as catheter may be higher. For a more definitive decision, further investigation is needed by examining pre- and post-hemodialysis evaluation in individuals with chronic kidney disease with and without hemodialysis.

ETHICAL DECLARATIONS

Ethics Committee Approval

The study was initiated after obtaining ethics committee approval from Yozgat Bozok University Non-interventional Clinical Researches Ethics Committee (Date: 09.04.2025, Decision No: 457).

Informed Consent

Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process

Externally peer-reviewed.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

Financial Disclosure

The authors declared that this study has received no financial support.

Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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